Potential bioterrorism agent: Category B

TYPHUS

DISEASE REPORTING

In Washington

The only form of typhus endemic to Washington is fleaborne typhus; the last reported case occurred in 1994.

Purpose of reporting and surveillance

- To educate people about how to reduce their risk of infection.
- To educate potentially exposed persons about signs and symptoms of disease, thereby facilitating early diagnosis.

Reporting requirements

- Health care providers: **immediately notifiable**
- Hospitals: **immediately notifiable**
- Laboratories: no requirements for reporting
- Local health jurisdictions: notifiable to DOH Communicable Disease Epidemiology within 7 days of case investigation completion or summary information required within 21 days. ***If bioterrorism is suspected, case must be immediately reported to DOH: 1-877-539-4344***

CASE DEFINITION FOR SURVEILLANCE

Clinical criteria for diagnosis

A febrile illness with temperature ≥100.5^{o}F (38.0^{o}C). A typical clinical presentation includes fever, chills, headache, myalgias, nausea, vomiting, and in 50%, a petechial or maculopapular rash. In the US, typhus may be seen in travelers to endemic areas, or following exposure to rodents fleas.

Laboratory criteria for diagnosis

- Fourfold rise in serum antibody titers to *Rickettsia* antigen, or
- *Rickettsia* detected in a clinical specimen by polymerase chain reaction (PCR) assay, or
- Identification of *Rickettsia* in tissue by immunohistochemical stain.

Case definition

- Probable: A case with a typical clinical presentation, with no established alternative diagnosis, but with a single positive *Rickettsia* immunoglobulin M (IgM) or immunoglobulin G (IgG) titer.
- Confirmed: A case that is laboratory confirmed, or a case that meets the clinical case definition and is not laboratory confirmed, but is epidemiologically linked to a confirmed case.

EPIDEMIC LOUSEBORNE TYPHUS FEVER

A. DESCRIPTION

1. Identification

A rickettsial disease with variable onset; often sudden and marked by headache, chills, prostration, fever and general pains. A macular eruption appears on the fifth to sixth day, initially on the upper trunk, followed by spread to the entire body, but usually not to the face, palms or soles. Toxemia is usually pronounced, and the disease terminates by rapid defervescence after about 2 weeks of fever. The case-fatality rate increases with age and varies from 10% to 40% in the absence of specific therapy. Mild infections may occur without eruption, especially in children and people partially protected by prior immunization. The disease may recrudesce years after the primary attack (Brill-Zinsser disease); this form of disease is milder, has fewer complications, and has a lower case-fatality rate.

The IF test is most commonly used for laboratory confirmation, but it does not discriminate between louseborne and murine typhus unless the sera are differentially absorbed with the respective rickettsial antigen prior to testing. Other diagnostic methods are EIA, PCR, immunohistochemical staining of tissues, CF with group specific or washed type specific rickettsial antigens, and the toxin-neutralization test. Antibody tests usually become positive in the second week. In acute disease, the initial antibody is IgM and in Brill-Zinsser disease, IgG.

2. Infectious Agent

Rickettsia prowazekii.

3. Worldwide Occurrence

In colder areas where people may live under unhygienic conditions and are louse infested; enormous and explosive epidemics may occur during war and famine. Endemic foci exist in mountainous regions of Mexico, Central and South America, in central and east Africa and numerous countries of Asia. In the US, the last outbreak of louseborne typhus occurred in 1921. This rickettsia exists as a zoonosis of flying squirrels (*Glaucomys volans*) and there is serologic evidence that humans have been infected from this source, possibly

by the squirrel flea. Most of these have been in the east coast states, cases have also been reported from Indiana, California, Illinois, Ohio, Tennessee and West Virginia.

4. Reservoir

Humans are the reservoir and are responsible for maintaining the infection during interepidemic periods. Although not a major source of human disease, sporadic cases may be associated with flying squirrels.

5. Mode of Transmission

The body louse, *Pediculus humanus corporis*, is infected by feeding on the blood of a patient with acute typhus fever. Patients with Brill-Zinsser disease can infect lice and may serve as foci for new outbreaks in louse infested communities. Infected lice excrete rickettsiae in their feces and usually defecate at the time of feeding. People are infected by rubbing feces or crushed lice into the bite or into superficial abrasions. Inhalation of infective louse feces in dust may account for some infections. Transmission from the flying squirrel is presumed to be by the bite of the squirrel flea, but this has not been documented.

6. Incubation period

From 1 to 2 weeks, commonly 12 days.

7. Period of communicability

The disease is not directly transmitted from person to person. Patients are infective for lice during the febrile illness and possibly for 2-3 days after the temperature returns to normal. Infected lice pass rickettsiae in their feces within 2-6 days after the blood meal; it is infective earlier if crushed. The louse invariably dies within 2 weeks after infection; rickettsiae may remain viable in the dead louse for weeks.

8. Susceptibility and resistance

Susceptibility is general. One attack usually confers long-lasting immunity.

B. METHODS OF CONTROL

1. Preventive measures:

a. Apply an effective residual insecticide powder at appropriate intervals by hand or power blower to clothes and persons of populations living under conditions favoring louse infestation. The lousicide used should be effective on local lice.
b. Improve living conditions with provisions for bathing and washing clothes.

c. Treat prophylactically those who are subject to risk, by application of residual insecticide to clothing by dusting or impregnation.

2. Control of patient, contacts and the immediate environment:

a. Report to local health authority.
b. Isolation: Not required after proper delousing of patient, clothing, living quarters and household contacts.
c. Concurrent disinfection: Appropriate insecticide powder applied to clothing and bedding of patient and contacts; launder clothing and bedclothes. Lice tend to leave abnormally hot or cold bodies in search of a normothermic clothed body (see B1a, above). If death from louseborne typhus occurs before delousing, delouse the body and clothing by thorough application of an insecticide.
d. Quarantine: Louse infested susceptibles exposed to typhus fever ordinarily should be quarantined for 15 days after application of an insecticide with residual effect.
e. Management of contacts: All immediate contacts should be kept under surveillance for 2 weeks.
f. Investigation of contacts and source of infection: Every effort should be made to trace the infection to the immediate source.
g. Specific treatment: A single dose of doxycycline 200 mg will usually cure patients in epidemic settings. Tetracyclines or chloramphenicol orally in a loading dose of 2-3 g, followed by daily doses of 1-2 g/day in 4 divided doses until the patient becomes afebrile (usually 2 days) plus 1 day. When faced with a seriously ill patient with possible typhus, suitable therapy should be started without waiting for laboratory confirmation.

3. Epidemic measures

The measure for rapid control of typhus is application of an insecticide with residual effect to all contacts. Where infestation is known to be widespread, systematic application of residual insecticide to all people in the community is indicated. Treatment of cases in an epidemic may also decrease the spread of disease.

4. International measures

a. Telegraphic notification by governments to WHO and to adjacent countries of the occurrence of a case or an outbreak of louseborne typhus fever in an area previously free of the disease.
b. International travelers: No country currently requires immunization against typhus for entry.
c. Louseborne typhus is a Disease under Surveillance by WHO. WHO Collaborating Centres.

ENDEMIC FLEABORNE TYPHUS FEVER

A. DESCRIPTION

1. Identification

A rickettsial disease whose course resembles that of louseborne typhus, but is milder. The case-fatality rate for all ages is less than 1% but increases with age. Absence of louse infestation, geographic and seasonal distribution and sporadic occurrence of the disease help to differentiate it from louseborne typhus. For laboratory diagnosis, see louseborne typhus fever, section A, above.

2. Infectious Agent

Rickettsia typhi (*Rickettsia mooseri*); *Rickettsia felis*.

3. Worldwide Occurrence

Worldwide. Found in areas where people and rats occupy the same buildings. In the US, fewer than 80 cases are reported annually. Seasonal peak occurs in late summer and autumn; cases tend to be scattered, but with a high proportion reported from Texas and southern California. Multiple cases may occur in the same household.

4. Reservoir

Rats, mice and possibly other small mammals. Infection is maintained in nature by a rat flea rat cycle where rats are the reservoir (commonly *Rattus rattus* and *R. norvegicus*) but infection is inapparent. A closely related organism, *Rickettsia felis*, has been found in a cat to cat flea to opossum cycle in southern California and probably occurs elsewhere.

5. Mode of Transmission

Infective rat fleas (usually *Xenopsylla cheopis*) defecate rickettsiae while sucking blood; this contaminates the bite site and other fresh skin wounds. An occasional case may follow inhalation of dried infective flea feces. Infection with *Rickettsia felis* occurs in opossums, cats, dogs and other wild and domestic animals; this is self-limited, but these animals may transport infective cat fleas, *Ctenocephalides felis* to humans.

6. Incubation period

From 1 to 2 weeks, commonly 12 days.

7. Period of communicability

Not directly transmitted from person to person. Once infected, fleas remain so for life (up to 1 year).

8. Susceptibility and resistance

Susceptibility is general. One attack confers immunity.

B. METHODS OF CONTROL

1. Preventive measures:

a. Apply insecticide powders with residual action to rat runs, burrows and harborages.
b. To avoid increased exposure of humans, wait until flea populations have first been reduced by insecticides before instituting rodent control measures (see Plague, B1b-B1c, B1f).

2. Control of patient, contacts and the immediate environment:

a. Report to local health authority.
b. Isolation: None.
c. Concurrent disinfection: None.
d. Quarantine: None.
e. Immunization of contacts: None.
f. Investigation of contacts and source of infection: Search for rodents or opossums around premises or home of patient.
g. Specific treatment: Tetracyclines (usually doxycycline) in daily oral or intravenous doses for 5-7 days and for at least 48 hours once the patient is afebrile. Chloramphenicol may also be used, but is administered only when there is an absolute contraindication for using tetracyclines. Treatment should be initiated on clinical and epidemiologic considerations without waiting for laboratory confirmation of the diagnosis.

3. Epidemic measures

In endemic areas with numerous cases, use of a residual insecticide effective against rat or cat fleas will reduce the flea index and the incidence of infection in humans.

4. International measures

WHO Collaborating Centres.

SCRUB TYPHUS

A. DESCRIPTION

1. Identification

A rickettsial disease often characterized by a primary punched out skin ulcer (eschar) corresponding to the site of attachment of an infected mite. An acute febrile onset follows within several days, along with headache, profuse sweating, conjunctival injection and lymphadenopathy. Late in the first week of fever, a dull red, maculopapular eruption appears on the trunk, extends to the extremities and disappears in a few days. Cough and x-ray evidence of pneumonitis are common. Without antibiotic therapy, fever lasts for about 14 days. The case-fatality rate in untreated cases varies from 1% to 60%, according to area, strain of rickettsia and previous exposure to disease; it is consistently higher among older people.

Definitive diagnosis is made by isolation of the infectious agent by inoculating the patient's blood into mice. Serologic diagnosis is complicated by antigenic differences of various strains of the causal rickettsia; the IF test is the preferred technique, but EIAs are also available. Many cases develop a positive Weil-Felix reaction with the Proteus OXK strain.

2. Infectious Agent

Orientia tsutsugamushi with multiple serologically distinct strains.

3. Worldwide Occurrence

Central, eastern and southeast Asia; from southeastern Siberia and northern Japan to northern Australia and Vanuatu, as far west as Pakistan, to as high as 10,000 feet above sea level in the Himalayan Mountains, and particularly prevalent in northern Thailand. Acquired by humans in one of innumerable small, sharply delimited “typhus islands,” some covering an area of only a few square feet, where rickettsiae, vectors and suitable rodents exist simultaneously. Occupation greatly influences the gender distribution; restricted mainly to adult workers who frequent scrub overgrown terrain or other mite infested areas, such as forest clearings, reforested areas, new settlements or even newly irrigated desert regions. Epidemics occur when susceptibles are brought into endemic areas, especially in military operations in which 20%-50% of troops have been infected within weeks or months.

4. Reservoir

Infected larval stages of trombiculid mites; *Leptotrombidium akamushi*, *L. deliensis* and related species (varying with area) are the most common vectors for humans. Infection is maintained by transovarian passage in mites.

5. Mode of Transmission

By the bite of infected larval mites; nymphs and adults do not feed on vertebrate hosts.

6. Incubation period

Usually 10-12 days; varies from 6 to 21 days.

7. Period of communicability

Not directly transmitted from person to person.

8. Susceptibility and resistance

Susceptibility is general. An attack confers prolonged immunity against the homologous strain of *O. tsutsugamushi* but only transient immunity against heterologous strains. Heterologous infection within a few months results in mild disease, but after a year produces typical illness. Second and even third attacks of naturally acquired scrub typhus (usually benign or inapparent) occur among people who spend their lives in endemic areas or who have not been completely treated (see below). No experimental vaccine has been effective.

B. METHODS OF CONTROL

1. Preventive measures:

a. Prevent contact with infected mites by personal prophylaxis against the mite vector, achieved by impregnating clothes and blankets with miticidal chemicals (permethrin and benzyl benzoate) and application of mite repellents (diethyltoluamide, Deet) to exposed skin surfaces.
b. Eliminate mites from the specific sites by application of chlorinated hydrocarbons, such as lindane, dieldrin or chlordane, to ground and vegetation in environs of camps, mine buildings and other populated zones in endemic areas.
c. In a small group of volunteers in Malaysia, the administration of 7 weekly doses of doxycycline (200 mg/week in a single dose) was an effective prophylactic regimen.

2. Control of patient, contacts and the immediate environment:

a. Report to local health authority.
b. Isolation: None.
c. Concurrent disinfection: None.
d. Quarantine: None.
e. Immunization of contacts: None.
f. Investigation of contacts and source of infection: None (see B3, below).

g. Specific treatment: One of the tetracyclines orally in a loading dose, followed by divided doses daily until patient is afebrile (average 30 hours). Chloramphenicol is equally effective and should be given if tetracyclines are contraindicated (see louseborne typhus fever section B2g, above). If treatment is started within the first 3 days of illness, recrudescence is likely unless a second course of antibiotic is given after an interval of 6 days. In Malaysia single doses of doxycycline (5 mg/kg) were effective when given on the seventh day, and in the Pescadores Islands (Taiwan area) when given on the fifth day; earlier administration was associated with some relapses. Azithromycin has also been used successfully in pregnant patients.

3. Epidemic measures

Rigorously employ procedures described in this section, B1a through B1b above, in the affected area; daily observation of all people at risk for fever and appearance of primary lesions; institute treatment on first indication of illness.

4. International measures

WHO Collaborating Centres.